

## **AMENDMENTS TO THE CLAIMS:**

The following listing of claims replaces all previous listing of claims.

1. (Withdrawn) A virus-like particle (VLP) comprising i) a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of an avian hepadnavirus large envelope polypeptide (L) or a functional derivative thereof and ii) an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof.
2. (Withdrawn) The VLP of claim 1 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of duck hepatitis B virus (DHBV), or a functional derivative thereof.
3. (Withdrawn) The VLP of claim 1 or 2 comprising a fusion polypeptide comprising a polypeptide of interest (POI) and a particle-associating portion of a large envelope polypeptide (L) of duck hepatitis B virus (DHBV), or a functional derivative thereof and ii) a small envelope (S) polypeptide of DHBV, or a functional derivative thereof.
4. (Withdrawn) The VLP of claim 1 or 2 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.
5. (Withdrawn) The VLP of claim 1 or 2 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
6. (Withdrawn-previously presented) The VLP of claim 1 or 2 wherein the L polypeptide comprises the amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof or comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 7 or SEQ ID NO: 9.

7. (Withdrawn-previously presented) The VLP of claim 1 wherein the particle-associating portion of L polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or a functional derivative thereof comprising an amino acid sequence having at least 90% identity to SEQ ID NO: 7 or SEQ ID NO: 9.
8. (Withdrawn-previously presented) The VLP of claim 1 or 2 wherein the particle-associating portion of L-polypeptide comprises or consists essentially of amino acids 24 to 107 of SEQ ID NO: 9 or an amino acid sequence having at least 90% identity thereto.
9. (Withdrawn) The VLP of claim 1 wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
10. (Withdrawn-previously presented) The VLP of claim 1 wherein said L polypeptide or particle-associating portion thereof is encoded by the sequence of nucleotides as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about 90% identity to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
11. (Withdrawn) The VLP of claim 1 or 2 wherein the L polypeptide further comprises a signal sequence.
12. (Canceled)
13. (Currently amended) A fusion polypeptide ~~for use in the assembly of a VLP comprising an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof,~~ said fusion polypeptide comprising a polypeptide of interest (POI) and at least fused to a particle-associating portion of a large envelope polypeptide (L) of an avian hepadnavirus wherein the POI is not a pre-S region of an avian hepadnavirus and is located N-terminally to said particle-associating portion of the L polypeptide, and wherein the particle-associating portion consists of a fragment of the L polypeptide, said fragment

~~comprising~~ comprises (i) the S domain of L, (ii) ~~the L polypeptide minus the preS domain or minus the TM1 domain,~~ (iii) the S domain minus the TM1 domain, or ~~(iv)~~ (iii) a portion of the L polypeptide which is downstream of TM1 and comprises at least TM2, the 5' cysteine loop between TM1 and TM2, and ~~sequences~~ the sequence downstream of TM2, ~~wherein the fusion polypeptide associates with said VLP comprising an avian hepadnavirus small envelope (S) polypeptide or a functional derivative thereof.~~

14. (Currently amended) The polypeptide of claim ~~12 or~~ 13 wherein the particle-associating portion of L consists of (i) the S domain of L, (ii) the S domain of L absent the TM1 domain, or (iii) a portion of the L polypeptide which is downstream of TM1 and comprises at least TM2, the 5' cysteine loop between TM1 and TM2, and ~~sequences~~the sequence downstream of TM2.
- 15 - 16. (Canceled)
17. (Currently amended) The polypeptide of claim ~~12 or~~ 13 wherein the particle-associating portion of L polypeptide consists of the amino acid sequence as set forth in SEQ ID NO: 9 or amino acid sequence having at least 90% identity to SEQ ID NO: 9 (S domain of L).
18. (Currently amended) The polypeptide of claim ~~12 or~~ 13 wherein the particle-associating portion of L-polypeptide consists essentially of amino acids 24 to ~~[[107]]~~167 of SEQ ID NO: 9 or an amino acid sequence having at least 90% identity thereto.
19. (Currently amended) The polypeptide of claim ~~12 or~~ 13 wherein said particle-associating portion thereof is encoded by the sequence of nucleotides as set forth in SEQ ID NO: 8 or having at least about 90% identity to SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 8 under hybridisation conditions of ~~medium~~moderate stringency.
20. (Currently amended) The polypeptide according to claim ~~12 or~~ 13 wherein said L polypeptide fusion protein further comprises a signal sequence.

21. (Currently amended) The polypeptide of claim ~~12~~ or 13 wherein the L polypeptide is a DHBV L polypeptide.
22. (Withdrawn) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding a fusion protein comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
23. (Withdrawn) A recombinant nucleic acid molecule for use in making a VLP, said nucleic acid molecule comprising a contiguous sequence of nucleotides encoding i) a fusion polypeptide comprising a polypeptide of interest (POI) and at least a particle-associating portion of an L polypeptide of an avian hepadnavirus or a functional derivative thereof, and ii) a small envelope (S) polypeptide of an avian hepadnavirus or a functional derivative thereof, wherein the POI is not a pre-S region of an avian hepadnavirus.
24. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the particle-associating portion of L comprises at least the S domain of L, or the S domain of L minus the TM1 domain, or a functional derivative thereof.
25. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the POI is located in the pre-S domain of L or at the amino terminal side of the S domain of L, or the S domain minus the TM1 domain of L.
26. (Withdrawn-previously presented) The nucleic acid molecule of claim 22 or 23 which encodes an L polypeptide comprising an amino acid sequence substantially as set forth in SEQ ID NO: 7 or SEQ ID NO: 9 or comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 7 or SEQ ID NO: 9.
27. (Withdrawn-previously presented) The nucleic acid molecule of claim 26 which encodes a

particle associating portion of L polypeptide consisting essentially of amino acids 24 to 167 of SEQ ID NO: 9 or an amino acid sequence having at least 90% identity to SEQ ID NO: 9.

28. (Withdrawn-previously presented) The nucleic acid molecule of claim 22 or 23 wherein said L polypeptide or particle associating portion thereof is encoded by a sequence of nucleotides as set forth in SEQ ID NO: 6 or SEQ ID NO: 8 or having at least about 90% identity to SEQ ID NO: 6 or SEQ ID NO: 8 or a contiguous sequence of nucleotides capable of hybridizing to a complementary form of SEQ ID NO: 6 or SEQ ID NO: 8 under hybridisation conditions of medium stringency.
29. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide further comprises a signal sequence.
30. (Withdrawn) The nucleic acid molecule of claim 22 or 23 wherein the L polypeptide is a DHBV L polypeptide or functional derivative thereof.
- 31-39. (Canceled)
40. (Withdrawn) An isolated and/or recombinant cell comprising the nucleic acid molecule of any one of claims 22 to 30 or expressing the polypeptide of any one of claims 12 to 21 or the VLP of any one of claims 1 to 11.
41. (Withdrawn) The cell according to claim 40 wherein said cell is a eukaryotic cell, preferably a yeast, avian or mammalian cell.
42. (Withdrawn) A method of delivering a POI to a subject or cell comprising expressing the POI in a VLP comprising L polypeptide from an avian hepadnavirus or a functional derivative thereof such that at least part of the POI is expressed on the surface of the VLP and administering the VLP to a subject or cell.

43. (Withdrawn) The method of claim 42 wherein the VLP is made in an *in vitro* expression system such as a yeast, avian or mammalian expression system.
44. (Withdrawn) The method of claim 42 wherein the VLP is made *in vivo* in the cells of a subject after administration of the nucleic acid molecule of any one of claims 22 to 30.
45. (Withdrawn) A method for making a recombinant VLP said method comprising:
- i) cloning a nucleic acid molecule encoding a polypeptide of interest into an expression vector comprising a particle-associating portion of an L polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof;
  - ii) introducing the recombinant expression vector of step i) into a suitable cell and maintaining same under conditions which allow protein expression and particle assembly with S polypeptide of an avian hepadnavirus, such as DHBV, or a functional derivative thereof; and
  - iii) recovering said virus-like particles from said cells.

46-47. (Canceled)